or even cause oncogenic mutations. Immunoglobulin E (IgE) is a class of antibody that binds to cells antigen-nonspecifically via specialized receptors (FcεRs) on mast cells, basophils, eosinophils, and monocytes. Cross-linking of IgE triggers production of ROI, which help to mediate the release of the inflammatory mediators histamine and eicosanoids (*5*). Perhaps IgE contributes further to mast cell activation by catalyzing formation of more potent oxidants. Furthermore, cells can bear antibody molecules when antibody is directed against an antigen on the cell surface, as in some forms of autoimmunity and immunotherapy. For example, patients with rheumatoid arthritis or an inflammatory bowel disorder called Crohn's disease may benefit from injection of antibodies against the cytokine tumor necrosis factor (TNF); those with rheumatoid arthritis may also benefit from injection of soluble TNF receptors. It is assumed that both reagents work by neutralizing TNF. However, TNF-specific antibody may also bind to activated macrophages, mast cells, and T cells that express TNF on their surface (*6*). Antibodies against leukocyte surface molecules can trigger production of ROI. Then, cell-bound antibody might convert these ROI into toxic forms, injuring the cells to which the antibody is attached and ameliorating inflammatory disease.

Immune complex disorders are also settings in which antibody is brought into proximity with $^1O_2^*$. For example, antigen-antibody complexes can accumulate in the glomeruli of the kidney and fix complement, attracting and activating phagocytes. In rheumatoid arthritis, affected joints contain rheumatoid factor, an antigen-antibody complex in which the antigen is itself antibody. The rheumatoid joint also holds large numbers of neutrophils that respond to TNF by releasing copious ROI (*7*). Rheumatoid factor may catalyze the conversion of these ROI to forms that inactivate protease inhibitors and damage the joint.

Finally, nonphagocytic cells produce ROI as second messengers in mitogenic and other signaling reactions. These reactions are mediated in part by a family of enzymes (NOXs) that includes the phagocyte oxidase (phox) responsible for ROI production by the innate immune system (*8*). Autoantibodies, therapeutic antibodies, and immune complexes may thus encounter $^1O_2^*$ produced by diverse cell types.

Like most discoveries, the Wentworth *et al.* (*3*) work leaves critical questions open for future investigation. The receptors for antibody (FcRs) expressed by neutrophils are not thought to retain antibody in the absence of antigen. Thus, the display of nonspecific antibody on the neutrophil surface suggested by the Wentworth *et al.* study requires explanation. The extent to which cell-bound antibody contributes to O_3 production by phagocytes or to their antibacterial activity has not yet been tested. The quantitative dependence of microbial killing on $H_2O_2 + O_3$ has not been defined or compared with the amounts of those products produced by antibody or by phagocytes with and without phagocyte-bound, bacteria-bound, or soluble antibody. It is not clear whether production of O_3 leads to more $^{\cdot}OH$ radical than phagocytes might form by other routes, such as the reaction of H_2O_2 with $^{\cdot}O_2^-$ (see the figure) or with ferrous or cuprous ions.

ENZYMATIC GENERATION OF PHYSIOLOGICALLY IMPORTANT GASES IN MAMMALS

Gas	Enzyme	Functions
$^{\cdot}O_2^-$	Phox, other NOXs	Killing; signaling (*8*)
$^{\cdot}NO$	NOX synthases	Killing; signaling (*1*)
CO	Heme oxygenase	Signaling (*12*)
O_3	Antibody	Killing (*3*); signaling?

The study by Wentworth *et al.* opens a new chapter in the book on the phagocyte oxidase, phox. The importance of phox in host defense is clear, because people genetically deficient in this enzyme are highly susceptible to infection (*9*). An even wider role for phox is revealed when a partially compensating enzyme, nitric oxide synthase–2, is also absent (*10*). Some have argued that phox acts indirectly to activate antibacterial proteases (*11*). That conclusion was based on the inefficiency of relatively stable phox products as antibacterial agents when tested in isolation. The Wentworth *et al.* findings remind us that it can be misleading to analyze the antibacterial efficacy of single, relatively stable phox products. Instead, the more evanescent products are the most powerful killers and arise from interactions among ROI. Now, the interacting products include a newcomer, O_3, that kills by itself and offers a facile route to $^{\cdot}OH$ production. Perhaps we will come to regard the antibody molecule as the seventh component of the phox complex (see the figure), as well as the fourth mammalian enzyme shown to produce a functionally important gas (see the table).

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PERSPECTIVES: ULTRACOLD MATTER

The Quest for Superfluidity in Fermi Gases

Lev Pitaevskii and Sandro Stringari

Over the past decade, studies of ultracold atomic gas clouds have yielded unprecedented insights into the quantum statistical properties of matter. Most studies have focused on boson gases. On page 2179 of this issue, O'Hara *et al.* (*1*) report an ultracold Fermi gas that may provide a test bed for new theories of Fermi systems, from high-temperature superconductors to neutron stars.

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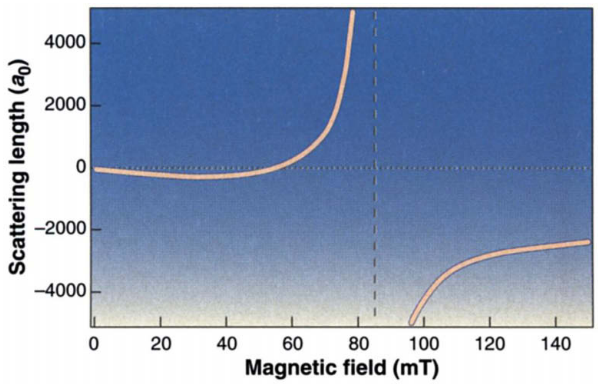
The elementary constituents of matter can be divided into fermions and bosons. Fermions are particles whose intrinsic angular momentum (or spin) is an odd multiple of $\hbar/2$, where $\hbar$ is the Planck constant divided by 2π. In contrast, the angular momentum of bosons is an even multiple of $\hbar/2$. The dramatically different thermodynamic properties of fermions and bosons at low temperature are a direct result of quantum statistical effects.

The fundamental constituents of atoms (electrons, neutrons, and protons) are fermions. However, pairs of fermions—and, in general, systems composed of an even number of fermions—behave like bosons. Because of their bosonic properties, hydrogen and several alkali elements can be used to study the phenomenon of Bose-Einstein condensation (2). But some isotopic species of these alkali atoms, like ^{6}Li and ^{40}K, with an odd number of fermions, instead exhibit fermionic behavior.

The first signatures of quantum statistical effects in atomic Fermi gases were reported in 1999 (3). An important motivation for these studies is the search for the transition to the superfluid phase (4), analogous to the transition exhibited by superconductors and liquid ^{3}He. According to the standard theory of fermion superfluidity, this transition should take place at extremely low temperatures, well below the Fermi temperature T_F (the typical temperature where quantum effects show up). Attempts to reach such temperatures with trapped atomic gases have encountered major difficulties because the cooling mechanisms become less and less efficient with decreasing temperature.



A change in value and sign. Scattering length for a mixture of the two lowest hyperfine states of ^{6}Li as a function of magnetic field. Lengths are given in units of the Bohr radius, a_0.

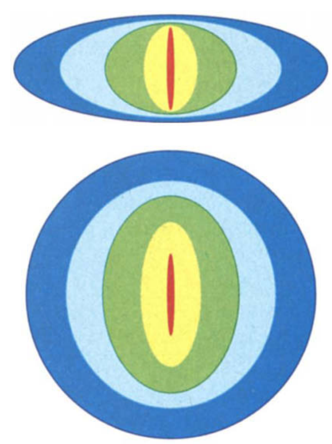
In contrast to other systems (such as atomic nuclei, liquid ^{3}He, and superconductors), the trapping and interaction mechanisms in atomic gases can be manipulated in a controlled manner, allowing the interaction between atoms to be tuned (5–7). By changing the strength of the magnetic field, the value and even the sign of the scattering length can be changed (see the first figure) (8). The scattering length can be extremely large, much larger than the average distance between atoms. As a result, the number of collisions increases dramatically, enhancing the efficiency of the cooling mechanisms, which are based on evaporation.

These large scattering lengths are not caused by a change in the range of the interatomic force, which is always small compared to the average distance between atoms, but by a bound molecular state (or resonance) close to the continuum. When the resonance is just below the continuum, the scattering length is large and positive. Conversely, when the resonance lies just above the continuum, the scattering length becomes large and negative.

It has recently been predicted (9–11) that these resonances provide a new type of superfluidity, called resonance superfluidity. Compared to traditional superfluidity, resonance superfluidity is predicted to occur at much higher temperatures, on the order of T_F.

O'Hara *et al.* now provide the first experimental realization of the resonance regime in a Fermi gas of ^{6}Li (1). Their experiment raises important questions about the many-body behavior of interacting Fermi systems. Among them, it is worth mentioning the problems of the unitarity limit in the collisional cross section and of superfluidity.

The unitarity limit in collisional processes is achieved when the modulus of the scattering length is much larger than the De Broglie wavelength of particles. In this limit, the scattering cross section, which characterizes the intensity of the interaction, reaches its maximum value, proportional to the square of the De Broglie wavelength of the colliding particles and independent of the value of the scattering length. First theoretical estimates (12) suggest that in the unitarity limit, many-body correlations result in an effective attractive interaction in atomic Fermi gases. The unitarity limit can also be formulated for a Bose gas (13), but at present there is no experimental evidence that a cold Bose gas is stable in the unitarity limit, in contrast to the Fermi gas.



Expansion of a cigar-shaped sample. (Top) Hydrodynamic regime. **(Bottom)** Collisionless regime. Different colors mark the shape of the gas at different expansion times.

The experiments of O'Hara *et al.* (1) were performed at 91 mT (910 G), where the scattering length has a large negative value (see the first figure). Under these conditions, the unitarity limit should be well achieved. Analysis of the expansion of the atomic cloud, carried out at the lowest temperatures, is consistent with theory, although the intensity of the effective interaction is found to be substantially smaller than predicted by theory. According to unitarity, the same result should hold for large positive values of the scattering length. Checking this behavior experimentally would provide further evidence that the unitarity limit has been reached.

The second challenging feature emerging from the experiment of (1) is the question of superfluidity. Menotti *et al.* recently suggested (14) that the anisotropy of the expanding gas, following the sudden release of the trap, could be used as a signature of superfluidity. In the superfluid regime, the macroscopic behavior of the gas is governed by the laws of irrotational hydrodynamics. If the gas is initially trapped by an anisotropic potential, during the expansion it will be accelerated more strongly in the direction of the short axis, where the confinement is tighter. As a consequence, if the shape of the atomic cloud is initially cigarlike, the expansion will convert it into a disk, and vice versa (15). This is exactly what O'Hara *et al.* have observed [see figure 1 of (1)] and differs dramatically from previous experiments on nonsuperfluid Fermi gases in the collisionless regime, where the asymptotic shape was found to be spherical, as predicted by collisionless ballistic expansion. The difference between hydrodynamic and collisionless expansions is illustrated schematically in the second figure.

The observation of anisotropic expansion can then be regarded as clear evidence of hydrodynamic behavior, where interactions play a major role. However, as O'Hara *et al.* (1) point out, this hydrodynamic regime can also be reached in the absence of superfluidity as a consequence of strong collisional effects in the normal phase. In fact, the collisional cross section can also be quite large at low temperatures, because the system is close to resonance.

Furthermore, the critical temperature for superfluidity is predicted (9–11) to be relatively high in the presence of resonance. Hence, both the normal and the superfluid phases may be governed by a hydrodynamic regime over the whole range of relevant temperatures. Under these conditions, no sharp transition to the superflu-

CREDIT: (TOP) GRAPH ADAPTED FROM (18); (BOTTOM) JOHN THOMAS, DUKE UNIVERSITY id phase can emerge from the analysis of the expansion of the gas.

Is it possible to probe directly the emergence of superfluidity in these ultracold Fermi gases? Measuring the collective oscillations is not expected to be of great help in this respect. The frequencies of the collective oscillations can provide an accurate check of the consequences of unitarity, but cannot distinguish whether the hydrodynamic regime is due to superfluidity or to collisional effects.

To probe directly the occurrence of superfluidity, one should investigate other quantum effects. An important example is the study of rotational phenomena, in particular quantized vortices. In superfluid Fermi systems, vortices are characterized by quanta of circulation that are multiples of $\pi\hbar$, in contrast to bosons, where the quanta are multiples of $2\pi\hbar$. By generating a single vortex line, aligned along the symmetry axis of the trap, one should be able to generate a configuration with angular momentum per particle equal to $\hbar/2$. Configurations with single vortex lines have been realized with Bose-Einstein condensed gases, probing directly the quantization of circulation (*16*). Repeating such an experiment in a Fermi gas should provide a stringent test of superfluidity.

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PERSPECTIVES: BEHAVIORAL ECOLOGY

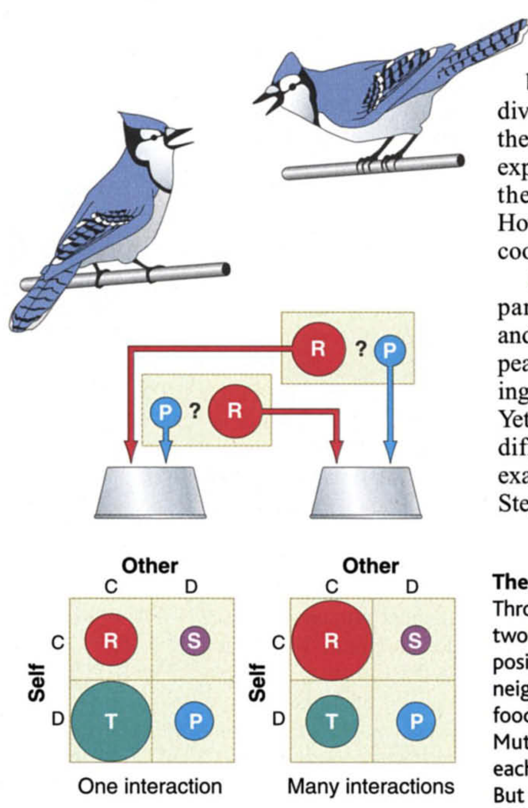
The Economics of Animal Cooperation

Michael Mesterton-Gibbons and Eldridge S. Adams

Human cooperation often depends on a delayed reciprocity in which each partner risks short-term costs to achieve a long-term mutual advantage. Are nonhuman animals capable of such cooperation? The evidence has been equivocal (*1*). However, in a set of clever experiments published on page 2216 of this issue, Stephens *et al.* (*2*) demonstrate that captive blue jays are indeed capable of sustained cooperation. Furthermore, the authors present evidence as to why it has been so difficult to observe sustained reciprocity in animal cooperation studies. In their experiment, a hungry bird can either cooperate or defect (that is, not cooperate) by selecting perches that control the allotment of seeds to itself and to a neighbor. Mutual cooperation allows both to obtain a large reward, whereas defection increases the immediate payoff to a selfish individual. By allowing food rewards to accumulate in clear trays before being released to the birds, the authors were able to control the degree to which their blue jay subjects preferred an immediate to a delayed reward (called discounting).

A large body of theory explores the potential for cooperation when there is a short-term temptation to cheat (*3*). Most of this theory builds on a thought experiment known as the Prisoner's Dilemma. In its simplest form, each of two individuals must "cooperate" (*C*) or "defect" (*D*)—that is, choose the option yielding the larger or the smaller payoff to the other. Mutual cooperation yields a higher reward (*R*) to each than does mutual defection (*P*) so that $R > P$ (see the figure). Yet each individual does better by defecting, regardless of the other individual's choice ($T > R$, $P > S$). So, in the absence of trust, each is tempted to exploit the other, and mutual defection is the only strategically stable outcome. How, then, can both enjoy the benefits of cooperation?

It has long been accepted that human partners can escape from this dilemma and sustain cooperation by interacting repeatedly and reciprocating (that is, matching the previous behavior of the other) (*4*). Yet such cooperation has been notoriously difficult to obtain in the laboratory. For example, in previous work, Clements and Stephens (*5*) exposed captive blue jays to



The Prisoner's Dilemma made simple. (Top) Through a system of levers and chutes, each of two hungry blue jays in adjoining cages can deposit either a large food item of value *R* in its neighbor's food tray (cooperation, *C*) or a small food item of value *P* in its own (defection, *D*). Mutual cooperation yields a higher reward to each than does mutual defection because $R > P$. But the temptation for each to exploit the other's cooperation by taking $R + P$ while the other gets nothing means that mutual defection is always strategically stable. **(Bottom left)** General reward matrix for a Prisoner's Dilemma: The rewards to one individual choosing *C* or *D* when the other chooses *C* or *D* satisfy $T > R > P > S$. The top part of the figure depicts the special case where $T = R + P$ and $S = 0$. **(Bottom right)** With a sufficient number of interactions, conditional cooperation increases the reward for mutual cooperation: Now $R > T$. But if the rewards reaped from cooperating are delayed, then the temptation to defect is eliminated only if $\alpha R > T$. Thus, as Stephens *et al.* (*2*) demonstrate, sustained cooperation may require both strategic reciprocity and sufficiently low discounting (sufficiently high α), that is, a sufficiently low preference for an immediate reward.

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